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Regularly Incremented Phase Encoding – Magnetic Resonance Fingerprinting (RIPE-MRF) for Enhanced Motion Artifact Suppression in Preclinical Cartesian MR Fingerprinting

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Abstract

Purpose—The Regularly Incremented Phase Encoding – Magnetic Resonance Fingerprinting (RIPE-MRF) method is introduced to limit the sensitivity of preclinical MRF assessments to pulsatile and respiratory motion artifacts.

Methods—As compared to previously reported standard Cartesian MRF methods (SC-MRF), the proposed RIPE-MRF method uses a modified Cartesian trajectory that varies the acquired phase encoding line within each dynamic MRF dataset. Phantoms and mice were scanned without gating or triggering on a 7T preclinical MRI scanner using the RIPE-MRF and SC-MRF methods. In vitro phantom T_1 and T_2 measurements as well as in vivo liver assessments of artifact-to-noise ratio (ANR) and MRF-based T_1 and T_2 mean and standard deviation were compared between the two methods ($n=5$).

Results—RIPE-MRF showed significant ANR reductions in regions of pulsatility ($P<0.005$) and respiratory motion ($P<0.0005$). RIPE-MRF also exhibited improved precision in T_1 and T_2 measurements in comparison to the SC-MRF method ($P<0.05$). The RIPE-MRF and SC-MRF methods displayed similar mean T_1 and T_2 estimates (difference in mean values $<10\%$).

Conclusion—These results show that the RIPE-MRF method can provide effective motion artifact suppression with minimal impact on T_1 and T_2 accuracy for in vivo small animal MRI studies.

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Keywords

Magnetic Resonance Fingerprinting; motion artifacts; artifact suppression; view ordering; Cartesian trajectory

INTRODUCTION

Quantitative preclinical MRI methods can be used to provide objective assessments of animal models of human disease for comparison with gold standard histological assessments (1–6). Unfortunately, quantitative imaging in small animals can be challenging due to anesthetized respiration rates of 40–80 breaths per minute and heart rates of >200 beats per minute causing blurring and ghosting artifacts that can result in quantification errors (4,5,7–11). Unfortunately, prospective respiratory/cardiac gating to reduce the motion artifacts (9,12–15) may not be practical because they can substantially extend acquisition times (16). Intubation and significant motion restriction (11,17) can also help reduce motion artifacts, but may cause increased mortality in animal models with advanced disease. As a result, preclinical respiratory and cardiovascular motion remains a significant challenge for accurate quantification in preclinical MRI studies.

Magnetic Resonance Fingerprinting (MRF) (18,19) is a quantitative MRI framework that has demonstrated unique properties including robustness to bulk patient motion and preclinical respiratory motion (18,20). However, this resistance to respiratory motion was only observed for low to moderate respiration rates. The same preclinical MRF study also showed that Cartesian MRF is susceptible to artifacts due to cardiac pulsatility. In this work, we propose the Regularly Incremented Phase Encoding (RIPE)-MRF methodology (21) for use on high field preclinical MRI scanners to suppress both respiratory and cardiac pulsatility motion artifacts. This new approach utilizes an incremented view ordering of the k-space phase encoding, within a fully-sampled Cartesian MRF trajectory, to reduce the impact of motion on the MRF-based T_1 and T_2 maps. The intention of the RIPE-MRF view ordering is to add temporal incoherence to the motion artifacts using altered k-space trajectories similar to the temporal incoherence instituted in highly undersampled non-Cartesian MRF (22–25). Herein, we compare the quantitative and motion suppression capabilities of this new RIPE-MRF technique to the previously described in vivo preclinical MRF methodology (20).

METHODS

RIPE-MRF Encoding

For this study, two Cartesian MRF methods were implemented on a Bruker Biospec 7T MRI Scanner (Bruker Inc., Billerica, MA). The previously described preclinical MRF method (20) will be referred to as Standard Cartesian MRF (SC-MRF). The RIPE-MRF method is derived from the SC-MRF method but has modified the acquisition order of the phase encoding lines as shown in Figure 1. The SC-MRF method (Fig. 1a) acquires the same phase encoding line during each variable repetition time for an entire set of dynamic MRF images. After acquiring the entire set of MRF data for this single phase encoding line, the phase encoding line is incremented and another set of dynamic MRF data is acquired. This process

is repeated for all phase encoding lines, starting with the edge line of k-space and continuing in a sequential fashion. In contrast, the RIPE-MRF method (Fig. 1b) linearly increments the acquired k-space line for each repetition time throughout the entire set of dynamic MRF images. The result of this phase encoding variation is a shuffled set of fully sampled Cartesian k-space time points that can be reordered to enable image reconstruction and quantification.

MRF Design and Quantification

Both the SC-MRF and RIPE-MRF acquisitions used a Fast Imaging with Steady-state Free Precession (FISP) imaging kernel (19,20) with patterns of flip angles and repetition times based on the original MRF method ((18) and Supporting Fig. S1). Following the MRF acquisitions, all imaging data were exported to MATLAB (The Mathworks, Natick, MA) for analysis. MRF quantification was performed by matching the acquired profiles on a pixel by pixel basis to a dictionary of simulated profiles from all logical combinations of T_1 and T_2 . For each pixel the maximum inner product between the acquired profile and the individual dictionary entry yielded the matched T_1 and T_2 values (26). M_0 was also estimated as a scale factor between the acquired data and simulated dictionary profile (18). In vitro MRF experiments were also performed to compare the accuracy of the T_1 and T_2 estimates from SC-MRF and RIPE-MRF with conventional spin echo MRI assessments (Supplemental Methods).

In vivo RIPE-MRF

All studies were conducted according to protocols approved by the CWRU Institutional Animal Care and Use Committee (IACUC). In vivo, single slice axial liver scans of wild type female C57BL/6 mice (8–12 weeks of age, $n=5$) were acquired sequentially using both SC-MRF and RIPE-MRF methods resulting in a set of T_1 , T_2 , and M_0 maps for each method. The order of the RIPE-MRF and SC-MRF scans was alternated between the animals to avoid potential bias due to the acquisition order (Supporting Fig. S2). Each mouse was scanned in two separate imaging sessions, using two different levels of anesthesia to evaluate the impact of respiration and heart rate on the two MRF methods. For the first imaging session, respiration was maintained at 45-60 breaths per minute by adjusting the depth of isoflurane anesthesia (high anesthesia state). The animals underwent a second imaging session with the respiration rate maintained at 80-100 breaths per minute (low anesthesia state). No gating or triggering was utilized so as to assess each method's baseline sensitivity to motion artifacts. Axial liver images were chosen to provide an MRF dataset with significant respiratory and pulsatile motion artifacts. Imaging parameters for the in vivo MRF studies were: 3×3 cm FOV, 128×128 matrix, and 1 mm slice thickness. The total imaging time for each mouse imaging session was 1.5 hours (45 minutes each for SC-MRF and RIPE-MRF).

We analyzed the SC-MRF and RIPE-MRF datasets to assess the effect of motion on the MRF signal evolution profiles. For this qualitative analysis, we utilized the magnitude of the signal intensity at the center of k-space for the MRF datasets which demonstrates both sensitivity to motion artifacts as well as limited noise levels in comparison to individual image voxels. An ideal dictionary profile was plotted with each acquired profile to illustrate

the appearance of deviations due to motion. In addition, composite MRF images were generated by taking the complex sum of the reconstructed dynamic MRF images across the entire time domain to visualize the temporal coherence of the motion artifacts for the RIPE-MRF and SC-MRF methods (Supporting Fig. S3). In these composite images incoherent noise should add destructively while coherent signals will add constructively highlighting any motion artifact coherence through time.

Coherence of the motion artifacts was quantified by manually selecting three ROIs in the background region of the composite images: 1) a region of pulsatility artifacts; 2) a region of respiratory motion artifacts; and 3) an overall artifact ROI with respiration and pulsatility artifacts. To ensure consistency, ROIs were selected to cover the entire background in the phase encoding direction for the desired region (Supporting Fig. S4). To measure the relative magnitude of motion artifacts (27), mean values for each of the artifact ROIs were divided by the mean of four separate ROIs taken in background regions with minimal motion artifacts to calculate an artifact-to-noise ratio (ANR). The ANR results from the RIPE-MRF and SC-MRF acquisitions were then compared using unpaired, two-tailed Student's t-tests.

A similar ROI analysis was also performed on the in vivo MRF-based T_1 and T_2 maps. Two ROIs were selected within the liver to compare the impact of the motion artifacts on the mean and standard deviation of the measured T_1 and T_2 values: 1) an area impacted by pulsatility artifact; and 2) an area impacted by respiratory motion artifact. To ensure consistency of the ROIs selection, the ROI for pulsatile motion artifact was chosen in the liver directly anterior to the aorta, while the ROI for respiratory motion artifact was chosen to be lateral to the pulsatile motion area (Supporting Fig. S4). The mean T_1 and T_2 value as well as the standard deviation for these ROIs as a percent of the mean value within the ROI were compared between corresponding areas from both methods using unpaired, Student's t-tests. MRF-based M_0 maps were analyzed separately in this study (Supporting Fig. S5) as M_0 is a scale factor while T_1 and T_2 are matched parameters. For all experiments, statistical significance was set at $P < 0.05$.

RESULTS

In Vivo Studies

Representative MRF profiles from SC-MRF and RIPE-MRF along with the dictionary profiles are shown in Figure 2 for both the high and low anesthesia states. The SC-MRF profiles exhibit regular coherent deviations from the matched dictionary profiles. For the RIPE-MRF profiles, these deviations are more distributed over the MRF profile and manifest as noise-like spikes. The temporal distribution of these motion-induced variations is consistent between the two anesthesia states, but more frequent in the low anesthesia state as expected.

Artifact-to-Noise Ratio (ANR) measurements from the ROI analysis of the in vivo composite MRF images (Supporting Fig. S3) are shown in Figure 3. ANR from the RIPE-MRF scans was significantly reduced in all ROIs for both anesthesia states in comparison to SC-MRF ($*P < 0.005$). The ANR was also reduced for the low anesthesia state compared to the high anesthesia state with significant differences seen between anesthesia states for SC-

MRF in the respiration and overall motion artifact regions ($*P < 0.005$) and in the overall motion artifact region for RIPE-MRF ($**P < 0.0005$).

Representative in vivo MRF-based T_1 and T_2 maps are shown in Figure 4 for both the high and low anesthesia states with parameter ranges chosen for display purposes. Consistent with ANR results, the in vivo SC-MRF maps exhibited visible motion artifacts in the phase encoding direction (blue and green arrows, Fig. 4). In contrast, the in vivo RIPE-MRF maps show visibly reduced artifacts both within the liver and in the background regions of the MRF maps. The ROI analysis of the MRF maps (Fig. 5) demonstrated that the mean parametric estimates were similar for both methods. The only significant difference was in mean T_1 values in the region of respiration artifact between anesthesia levels for RIPE-MRF (Fig. 5a, $*P < 0.05$). The spatial standard deviation in the parametric values as a percentage of the mean was generally reduced in the RIPE-MRF maps in comparison to SC-MRF suggesting improved uniformity of the RIPE-MRF maps. In particular, RIPE-MRF exhibited significantly reduced variation in three out of four regions with pulsatility artifacts (Fig. 5c,d, $*P < 0.05$). The corresponding M_0 maps are presented in Supporting Figure S5 and these demonstrate similar artifact patterns as the T_1 and T_2 maps.

Results of phantom studies showed significant differences between spin echo and both MRF methods. The MRF methods over-estimated the mean phantom T_1 values in comparison to conventional spin echo methods. In addition, the RIPE-MRF method showed small but significant reduction in mean T_2 values in comparison to both SC-MRF and the spin echo methods (Supporting Fig. S6).

DISCUSSION

Herein, we describe the Regularly Incremented Phase Encoding (RIPE) – MRF scheme to suppress respiratory and pulsatile motion artifacts in preclinical MRF applications. The RIPE-MRF approach attempts to decrease the temporal coherence of motion artifacts by varying the acquired k-space line during the MRF acquisition (Fig. 1). Linear increments in the phase encoding line were added during the dynamic MRF acquisition resulting in significant reductions in the coherence of motion artifacts (Figs. 2-3, Supporting Fig. S3). The application of modified view ordering to minimize the effect of motion artifacts has been previously used to improve image quality (28–31). The goal of this work was to utilize the concept of view ordering within the MRF framework to limit the impact of motion artifacts on the resulting quantitative maps. Subsequently, we show that this new RIPE-MRF trajectory provides a significant reduction in the coherence of motion artifacts resulting in more precise in vivo T_1 and T_2 measurements (Figs. 4, 5) compared to previously reported preclinical MRF methods (20).

In vivo application of the RIPE-MRF methodology altered the temporal distribution of motion artifacts in the MRF profiles (Fig. 2). While the periodic, motion-induced deviations in the MRF profiles are coherent for SC-MRF, RIPE-MRF deviations are “noise-like” displacements that are more evenly distributed across the entire MRF signal evolution profile. ANR measurements (Fig. 3) and composite images (Supporting Fig. S3) show these differences in the image domain. The reordering of the k-space datasets with RIPE-MRF

limited the temporal coherence of the motion artifacts and resulted in significantly reduced ANR. Importantly, these ANR reductions were consistent for both pulsatility and respiratory motion artifacts and for both high and low anesthesia states.

Motion-induced artifacts in the MRF signal evolution profiles also resulted in corresponding alterations in the MRF-based T_1 and T_2 maps. In vivo RIPE-MRF maps demonstrated a visible reduction in the appearance of motion artifacts in the liver compared to SC-MRF maps (Fig. 4). The impact of adding temporal incoherence to the motion artifacts on MRF-based quantification was manifest through reduced variation in the hepatic T_1 and T_2 values measured by RIPE-MRF in both regions of respiration and pulsatility artifacts (Fig. 5). Further, RIPE-MRF resulted in improved precision for both levels of anesthesia indicating it is effective in improving quantification over a range of physiological states. Both MRF methods resulted in mean hepatic T_1 estimates consistent with previous reports (4,17). Liver T_2 estimates from both MRF methods were reduced in comparison to reported literature values (11,17). This T_2 underestimation was also observed for the MRF phantom results in comparison to conventional MRI techniques (Supporting Fig. S6). T_2 underestimation may be partially ameliorated through corrections to B_0 and B_1 heterogeneities but were not further explored in this initial study.

The primary advantage of the RIPE-MRF method is eliminating the need for gating/triggering to get artifact free quantitative maps in small animal imaging. Prior preclinical studies have performed self-navigation and/or motion correction (32–35), retrospectively identified corrupted data using monitoring systems (7,36), or triggered the acquisition during the quiescent period of motion (16,37). These methods reduce motion artifacts but also significantly increase scan time and/or require complex post-processing. In contrast, RIPE-MRF provides a straightforward quantification process utilizing all available data with no restrictions. Additionally, the method is robust across a range of physiological motion rates reducing the need for precise physiological controls (i.e., intubation). Higher variation in the MRF maps in the regions of high frequency pulsatility artifacts indicate that the frequency of motion artifacts is an important factor in MRF trajectory design. For example, further reductions in motion artifacts may be needed to provide reliable MRF maps in regions with high-frequency / rapid motion (e.g., pulmonary / cardiac imaging). Therefore, future studies will be needed to investigate alternative view ordering methods (e.g., random phase encoding) and / or gated MRF approaches to provide artifact-free MRF-based T_1 and T_2 maps (23).

In this initial study, non-Cartesian trajectories were not explored as a potential form of motion suppression. Prior preclinical studies incorporating non-Cartesian trajectories, such as PROPELLER (2,38), spiral (16,37,39,40), and radial (41–43) k-space sampling, show promising motion artifact suppression. However, the resistance of non-Cartesian MRF methods to motion must be balanced with additional error sources such as eddy current - induced trajectory errors (44) and off-resonance artifacts prevalent on high field preclinical MRI scanners (16). From a practical perspective, non-Cartesian trajectories may be difficult or even impossible to implement on some preclinical MRI scanners. Further, this Cartesian RIPE-MRF approach may be useful for both preclinical and clinical MRF applications in combination with established parallel imaging strategies (45). Regardless, future studies will

be needed to thoroughly compare the relative motion artifact resistance of the Cartesian RIPE-MRF approach with non-Cartesian MRF trajectories.

CONCLUSIONS

In conclusion, we have developed the motion artifact-resistant RIPE-MRF method to provide reliable multi-parametric quantification for preclinical MRF applications. In this initial implementation, incrementing the phase encoding line during the dynamic MRF acquisition resulted in suppression of both pulsatility and respiratory motion artifacts in the in vivo MRF-based T_1 and T_2 relaxation time maps of mouse abdomens. This improved resistance to motion artifacts was achieved with no change in the MRF acquisition time as well as minimal impact on the accuracy of the T_1 and T_2 estimates. The RIPE-MRF method represents a shift in the preclinical quantitative imaging paradigm, from attempting to reduce or eliminate motion artifacts in the underlying images to accepting the presence of motion artifacts but manipulating them so they are suppressed during quantification. Thus, the RIPE-MRF method serves as a foundation for free-breathing Cartesian MRF in rodents.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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FIG. 1.

Schematic representation of two different MRF acquisition schemes. **(a)** Standard Cartesian MRF (SC-MRF) and **(b)** RIPE-MRF phase encoding schema showing four (out of 1024) MRF k-space time points. The red line in each time point dataset is acquired during the first set of dynamic MRF images (1024 total k-space lines). The blue line is the phase encoding line acquired during the second set of dynamic MRF images (second set of 1024 k-space lines). The green line is the third set of acquired MRF phase encoding lines. SC-MRF acquires the same phase encoding line during each set of dynamic MRF images, while the RIPE-MRF strategy increments the acquired phase encoding line during each set of dynamic MRF images to provide temporal incoherence for respiratory and pulsatile motion artifacts.

FIG. 2.

Comparison of MRF signal profiles. Signal intensity profiles from the center of k-space for the MRF datasets are shown with the corresponding dictionary entry overlaid. Profiles from SC-MRF and RIPE-MRF for both the (a) high and (b) low anesthesia states highlight differences in the appearance of motion between the methods. SC-MRF profiles show coherent deviations due to motion, while the RIPE-MRF profiles exhibit “noise-like” deviations distributed more evenly throughout the profile. The frequency of these deviations is increased in the high anesthesia state (b) as expected.

FIG. 3.

Artifact-to-noise ratios (ANR) for SC-MRF and RIPE-MRF. An ROI analysis was used on composite MRF images to measure mean ANRs for each MRF acquisition. Three regions corresponding to predominantly pulsatile motion artifacts, predominantly respiratory motion artifacts, and an overall motion artifact were analyzed. Noise ROIs were selected from motion-free regions of the image background. The RIPE-MRF method exhibited significantly reduced ANR for both the high and low anesthesia states in the regions of pulsatility ($**P < 0.0005$, $*P < 0.005$, respectively), respiration ($**P < 0.0005$, $**P < 0.0005$, respectively), and overall ($***P < 0.00005$, $**P < 0.0005$, respectively) motion artifacts in comparison to SC-MRF. The high and low anesthesia states showed significant differences within a method in the area of overall motion artifact for both SC-MRF and RIPE-MRF ($*P < 0.005$, $**P < 0.0005$, respectively) and in SC-MRF in the area of respiration artifact ($*P < 0.005$).

FIG. 4.

Representative T_1 (a) and T_2 (b) relaxation time maps of a healthy mouse liver. Example axial in vivo SC-MRF and RIPE-MRF maps, acquired sequentially in the same imaging session, are shown for both the high and low anesthesia states. Pervasive motion artifacts are seen in the phase encoding direction of the SC-MRF maps. The green arrow highlights an area of predominantly pulsatile motion artifacts in the SC-MRF scan while the blue arrow shows an area impacted by respiratory motion artifact. These artifacts are minimized in the RIPE-MRF maps and the areas appear more homogeneous.

FIG. 5.

Liver ROI T₁ and T₂ measurement analysis. Mean and standard deviation as a percentage of mean value for in vivo liver T₁ (a,c) and T₂ (b,d) values obtained from the SC-MRF and RIPE-MRF maps in regions of predominantly pulsatile and respiratory motion artifact (green and blue arrows respectively in Fig. 4) for both high and low anesthesia states. Statistically significant differences in T₁ relaxation time were seen between high and low anesthesia states in the area of respiration motion for RIPE-MRF (* $P < .05$). RIPE-MRF demonstrates more precise estimates of T₁ and T₂ as measured by the reduction in the spatial standard deviation of the measurements. For the RIPE-MRF assessments, the standard deviation was significantly reduced in three out of four T₁ comparisons to SC-MRF (* $P < 0.05$) and one of the four comparisons in T₂ (* $P < 0.05$). The low anesthesia state resulted in increased variation for all comparisons, but only the area of respiration artifact in T₂ was statistically significant for both SC-MRF and RIPE-MRF (*** $P < 0.0005$, ** $P < 0.005$, respectively).